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NOTICE OF ALLOWANCE AND FEE(S) DUE

65778 7590 08/13/2008

MCDONNELL, BOEHNEN, HULBERT AND BERGHOFF, LLP
300 SOUTH WACKER DRIVE
SUITE 3100
CHICAGO, IL 60606

EXAMINER

OLSON, ERIC

ART UNIT

PAPER NUMBER

1623

DATE MAILED: 08/13/2008

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/780,447	02/13/2004	Chandra Vargeese	MBHB02-312-G (600.041)	2130

TITLE OF INVENTION: CONJUGATES AND COMPOSITIONS FOR CELLULAR DELIVERY

APPLN. TYPE	SMALL ENTITY	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	YES	\$720	\$300	\$0	\$1020	11/13/2008

THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. PROSECUTION ON THE MERITS IS CLOSED. THIS NOTICE OF ALLOWANCE IS NOT A GRANT OF PATENT RIGHTS. THIS APPLICATION IS SUBJECT TO WITHDRAWAL FROM ISSUE AT THE INITIATIVE OF THE OFFICE OR UPON PETITION BY THE APPLICANT. SEE 37 CFR 1.313 AND MPEP 1308.

THE ISSUE FEE AND PUBLICATION FEE (IF REQUIRED) MUST BE PAID WITHIN THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. THIS STATUTORY PERIOD CANNOT BE EXTENDED. SEE 35 U.S.C. 151. THE ISSUE FEE DUE INDICATED ABOVE DOES NOT REFLECT A CREDIT FOR ANY PREVIOUSLY PAID ISSUE FEE IN THIS APPLICATION. IF AN ISSUE FEE HAS PREVIOUSLY BEEN PAID IN THIS APPLICATION (AS SHOWN ABOVE), THE RETURN OF PART B OF THIS FORM WILL BE CONSIDERED A REQUEST TO REAPPLY THE PREVIOUSLY PAID ISSUE FEE TOWARD THE ISSUE FEE NOW DUE.

HOW TO REPLY TO THIS NOTICE:

I. Review the SMALL ENTITY status shown above.

If the SMALL ENTITY is shown as YES, verify your current SMALL ENTITY status:

A. If the status is the same, pay the TOTAL FEE(S) DUE shown above.

B. If the status above is to be removed, check box 5b on Part B - Fee(s) Transmittal and pay the PUBLICATION FEE (if required) and twice the amount of the ISSUE FEE shown above, or

If the SMALL ENTITY is shown as NO:

A. Pay TOTAL FEE(S) DUE shown above, or

B. If applicant claimed SMALL ENTITY status before, or is now claiming SMALL ENTITY status, check box 5a on Part B - Fee(s) Transmittal and pay the PUBLICATION FEE (if required) and 1/2 the ISSUE FEE shown above.

II. PART B - FEE(S) TRANSMITTAL, or its equivalent, must be completed and returned to the United States Patent and Trademark Office (USPTO) with your ISSUE FEE and PUBLICATION FEE (if required). If you are charging the fee(s) to your deposit account, section "4b" of Part B - Fee(s) Transmittal should be completed and an extra copy of the form should be submitted. If an equivalent of Part B is filed, a request to reapply a previously paid issue fee must be clearly made, and delays in processing may occur due to the difficulty in recognizing the paper as an equivalent of Part B.

III. All communications regarding this application must give the application number. Please direct all communications prior to issuance to Mail Stop ISSUE FEE unless advised to the contrary.

IMPORTANT REMINDER: Utility patents issuing on applications filed on or after Dec. 12, 1980 may require payment of maintenance fees. It is patentee's responsibility to ensure timely payment of maintenance fees when due.

PART B - FEE(S) TRANSMITTAL

**Complete and send this form, together with applicable fee(s), to: Mail Mail Stop ISSUE FEE
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INSTRUCTIONS: This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 5 should be completed where appropriate. All further correspondence including the Patent, advance orders and notification of maintenance fees will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications.

CURRENT CORRESPONDENCE ADDRESS (Note: Use Block 1 for any change of address)

Note: A certificate of mailing can only be used for domestic mailings of the Fee(s) Transmittal. This certificate cannot be used for any other accompanying papers. Each additional paper, such as an assignment or formal drawing, must have its own certificate of mailing or transmission.

65778 7590 08/13/2008

MCDONNELL, BOEHNEN, HULBERT AND BERGHOFF, LLP
300 SOUTH WACKER DRIVE
SUITE 3100
CHICAGO, IL 60606

Certificate of Mailing or Transmission

I hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Mail Stop ISSUE FEE address above, or being facsimile transmitted to the USPTO (571) 273-2885, on the date indicated below.

(Depositor's name)
(Signature)
(Date)

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/780,447	02/13/2004	Chandra Vargeese	MBHB02-312-G (600.041)	2130

TITLE OF INVENTION: CONJUGATES AND COMPOSITIONS FOR CELLULAR DELIVERY

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nonprovisional	YES	\$720	\$300	\$0	\$1020	11/13/2008

EXAMINER	ART UNIT	CLASS-SUBCLASS
OLSON, ERIC	1623	514-054000

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).

☐ Change of correspondence address (or Change of Correspondence Address form PTO/SB/122) attached.

☐ "Fee Address" indication (or "Fee Address" Indication form PTO/SB/47; Rev 03-02 or more recent) attached. **Use of a Customer Number is required.**

2. For printing on the patent front page, list

(1) the names of up to 3 registered patent attorneys or agents OR, alternatively, 1 _____

(2) the name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed. 2 _____

3 _____

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. If an assignee is identified below, the document has been filed for recordation as set forth in 37 CFR 3.11. Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE

(B) RESIDENCE: (CITY and STATE OR COUNTRY)

Please check the appropriate assignee category or categories (will not be printed on the patent) : ☐ Individual ☐ Corporation or other private group entity ☐ Government

4a. The following fee(s) are submitted:

- ☐ Issue Fee
☐ Publication Fee (No small entity discount permitted)
☐ Advance Order - # of Copies _____

4b. Payment of Fee(s); (Please first reapply any previously paid issue fee shown above)

- ☐ A check is enclosed.
☐ Payment by credit card. Form PTO-2038 is attached.
☐ The Director is hereby authorized to charge the required fee(s), any deficiency, or credit any overpayment, to Deposit Account Number _____ (enclose an extra copy of this form).

5. **Change in Entity Status** (from status indicated above)

- ☐ a. Applicant claims SMALL ENTITY status. See 37 CFR 1.27. ☐ b. Applicant is no longer claiming SMALL ENTITY status. See 37 CFR 1.27(g)(2).

NOTE: The Issue Fee and Publication Fee (if required) will not be accepted from anyone other than the applicant; a registered attorney or agent; or the assignee or other party in interest as shown by the records of the United States Patent and Trademark Office.

Authorized Signature _____

Date _____

Typed or printed name _____

Registration No. _____

This collection of information is required by 37 CFR 1.311. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, Virginia 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/780,447	02/13/2004	Chandra Vargeese	MBHB02-312-G (600 041)	2130
65778	7590	08/13/2008	EXAMINER	
MCDONNELL, BOEHNEN, HULBERT AND BERGHOFF, LLP 300 SOUTH WACKER DRIVE SUITE 3100 CHICAGO, IL 60606			OLSON, ERIC	
			ART UNIT	PAPER NUMBER
			1623	
DATE MAILED: 08/13/2008				

Determination of Patent Term Adjustment under 35 U.S.C. 154 (b) (application filed on or after May 29, 2000)

The Patent Term Adjustment to date is 322 day(s). If the issue fee is paid on the date that is three months after the mailing date of this notice and the patent issues on the Tuesday before the date that is 28 weeks (six and a half months) after the mailing date of this notice, the Patent Term Adjustment will be 322 day(s).

If a Continued Prosecution Application (CPA) was filed in the above-identified application, the filing date that determines Patent Term Adjustment is the filing date of the most recent CPA.

Applicant will be able to obtain more detailed information by accessing the Patent Application Information Retrieval (PAIR) WEB site (<http://pair.uspto.gov>).

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Customer Service Center of the Office of Patent Publication at 1-(888)-786-0101 or (571)-272-4200.

Notice of Allowability

Application No.

10/780,447

Examiner

Eric S. Olson

Applicant(s)

VARGESE ET AL.

Art Unit

1623

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to Applicant's appeal brief submitted May 21, 2008.
2. ☒ The allowed claim(s) is/are 5, 6, 20, and 21.
3. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some* c) ☐ None of the:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).
- * Certified copies not received: ____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.

THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
- (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
- 1) ☐ hereto or 2) ☐ to Paper No./Mail Date ____.
- (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date ____.
- Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).**
6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

- | | |
|--|---|
| 1. <input type="checkbox"/> Notice of References Cited (PTO-892) | 5. <input type="checkbox"/> Notice of Informal Patent Application |
| 2. <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 6. <input type="checkbox"/> Interview Summary (PTO-413),
Paper No./Mail Date ____. |
| 3. <input type="checkbox"/> Information Disclosure Statements (PTO/SB/08),
Paper No./Mail Date ____ | 7. <input checked="" type="checkbox"/> Examiner's Amendment/Comment |
| 4. <input type="checkbox"/> Examiner's Comment Regarding Requirement for Deposit
of Biological Material | 8. <input checked="" type="checkbox"/> Examiner's Statement of Reasons for Allowance |
| | 9. <input type="checkbox"/> Other ____. |

/Shaojia Anna Jiang, Ph.D./
Supervisory Patent Examiner, Art Unit 1623

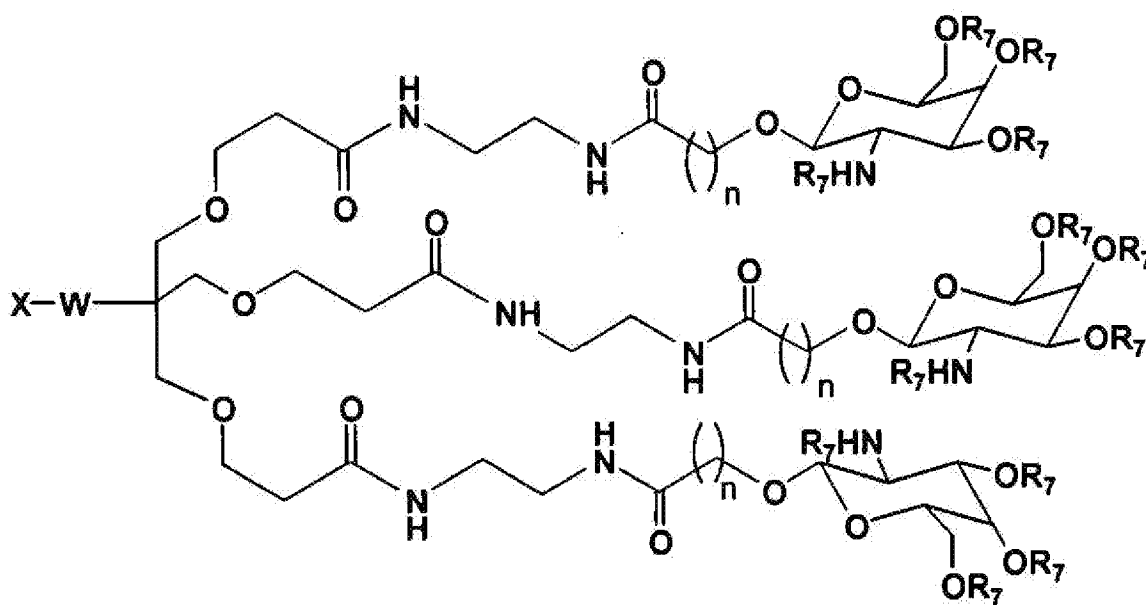
Examiner's Amendment

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was granted in a telephone interview by Christopher Singer on August 4, 2008.

Claims 5 and 6 are amended as follows:

5. (Currently Amended) A compound having Formula 119:



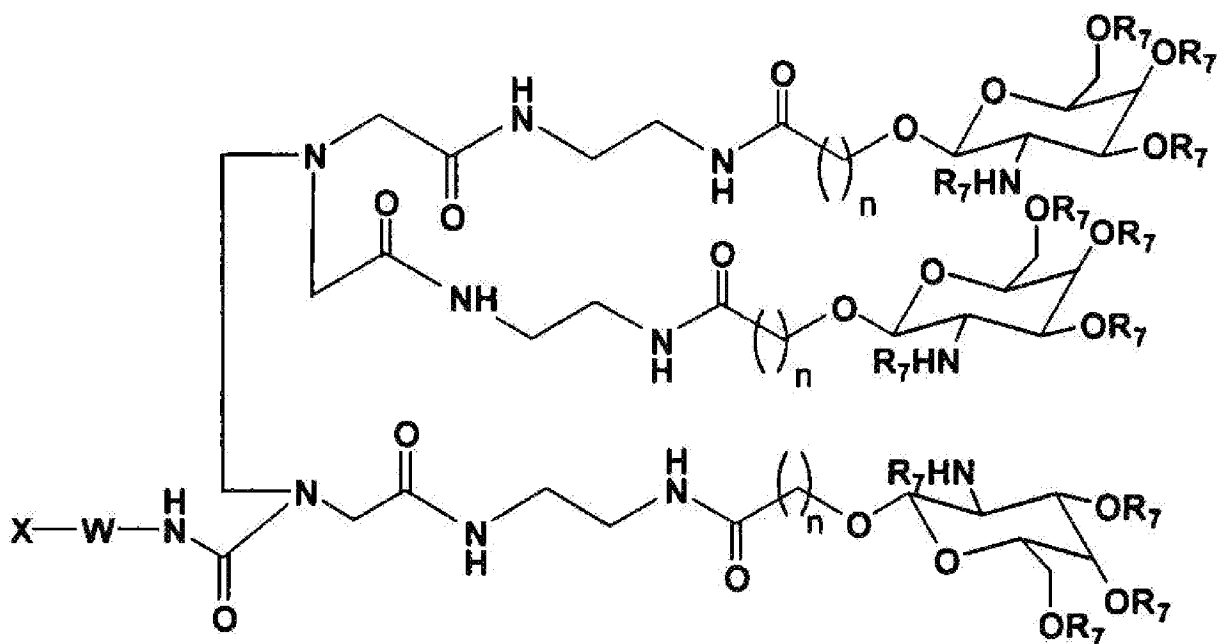
119

wherein X comprises a short interfering RNA (siRNA) molecule; W comprises a linker molecule or chemical linkage that can be present or absent, selected from the

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group consisting of amide, phosphate, phosphate ester, phosphoramidate, or thiophosphate ester linkage, each R7 independently comprises an acyl group that can be present or absent, and each n is independently an integer from about 1 to about 20.

6. (Currently Amended) A compound having Formula 121



121

wherein X comprises a short interfering RNA (siRNA) molecule; W comprises a linker molecule or chemical linkage that can be present or absent, selected from the group consisting of amide, phosphate, phosphate ester, phosphoramidate, or thiophosphate ester linkage, each R7 independently comprises an acyl group that can be present or absent, and each n is independently an integer from about 1 to about 20.

Claims 15 and 16 are cancelled.

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Claims 20 and 21 are amended as follows:

20. (Currently Amended) The compound of claim ~~540~~, wherein said siNA molecule comprises a sense strand and an antisense strand, and wherein said sense strand is conjugated with a compound comprising Formula 119.

21. (Currently Amended) The compound of claim ~~644~~, wherein said siNA molecule comprises a sense strand and an antisense strand, and wherein said sense strand is conjugated with a compound comprising Formula 121.

Detailed Action

This office action is a response to applicant's Appeal Brief submitted May 21, 2008.

This application is a continuation in part of 10/427160, currently pending, filed April 30, 2003, currently pending, which is a continuation in part of PCT/US02/15876, filed May 17, 2002, which claims benefit of provisional applications: 60/292217, filed May 18, 2001, 60/306883, filed July 20, 2001, 60/311865, filed August 13, 2001, and 60/362016, filed March 6, 2002. This application is also a continuation-in-part of PCT/US03/05346, filed February 20, 2003, and PCT/US03/05028, filed February 20, 2003, which claims benefit of the following provisional applications: 60/358580, filed February 20, 2002, 60/363124, filed March 11, 2002, 60/386782, filed June 6, 2002, 60/406784, filed August 29, 2002, 60/408378, filed September 5, 2002, 60/409293, filed September 9, 2002, and 60/440129, filed January 15, 2003.

However, the above priority documents PCT/US02/15876, filed May 17, 2002, 60/292217, filed May 18, 2001, 60/306883, filed July 20, 2001, 60/311865, filed August 13, 2001, 60/362016, filed March 6, 2002, PCT/US03/05346, filed February 20, 2003, PCT/US03/05028, filed February 20, 2003, 60/358580, filed February 20, 2002, 60/363124, filed March 11, 2002, 60/386782, filed June 6, 2002, 60/406784, filed August 29, 2002, 60/408378, filed September 5, 2002, 60/409293, filed September 9, 2002, and 60/440129, filed January 15, 2003, upon which priority is claimed fail to provide adequate support under 35 USC 112, first paragraph for the claimed subject

matter of instant claims 5, 6, 15, 16, 20, and 21 of this application because these provisional applications are not seen to disclose any conjugates comprising a galactosamine cluster glycoside moiety. Thus, the filing date of the instant claims is deemed to be the filing date of the parent application 10/427160, April 30, 2003. If applicant disagrees, applicant should present a detailed analysis as to why the claimed subject matter has clear support in the earlier priority applications. Applicant is reminded that such priority for the instant limitations requires written description and enablement under 35 U.S.C. § 112, first paragraph.

Claims 5, 6, 20, and 21 are pending in this application.

Claims 5, 6, 20, and 21 as amended are examined on the merits herein.

Reasons for Allowance

In view of the arguments presented in Applicant's appeal brief submitted May 21, 2008, the rejection of instant claims 5, 6, 15, 16, 20, and 21 under 35 USC 103(a) as being obvious over Low et al. in view of Connolly in view of Li et al. is withdrawn. The finality of the previous office action is withdrawn. Specifically, the above references do not disclose conjugates having the disclosed linking moieties.

Claims 5, 6, 20, and 21 are pending in this application and have been examined on the merits herein. Claims 5, 6, 20, and 21 are seen to be allowable. Reasons for allowance are given below:

The claimed compounds of structures 119 and 121 are seen to be adequately described and enabled by Applicant's specification. For example, pp. 55-58 disclose nucleic acid – cluster glycoside conjugates which provide written description for the claimed structures. Pp. 139-140 describe therapeutic and diagnostic uses of these compounds. Figures 46-48 in the drawings provide synthetic schemes that enable one skilled in the art to make the inventive compounds. Therefore the claimed invention meets the requirements of 35 USC 112.

Furthermore the claimed invention is novel and non-obvious over the prior art. Although it is known in the prior art to conjugate biological molecules such as RNA to molecules such as N-acetylgalactosamine cluster glycosides, as disclosed by the prior art references Low et al. and Connolly et al., the prior art does not disclose either of the specific linker compounds 119 or 121 as linkers used to conjugate two active moieties to one another. Furthermore, one of ordinary skill in the art would not have had any motivation to use either of these specific structures as linker moieties in this application, as evidenced by the lack of any suggestion in the prior art to use them as such. Therefore the claimed invention is seen to be novel and non-obvious over the prior art.

Therefore for these reasons, the claimed invention is seen to satisfy the requirements of 35 USC 112, 102, and 103.

Accordingly, the arguments presented in the appeal brief submitted May 21, 2008, and the accompanying examiner's amendment, are sufficient to remove all

rejections made in the prior office action as discussed above and to place the application in condition for allowance.

Any comments considered necessary by Applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled, "Comments on Statement of Reasons for Allowance."

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eric S. Olson whose telephone number is 571-272-9051. The examiner can normally be reached on Monday-Friday, 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Anna Jiang can be reached on (571)272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Eric S Olson/

Examiner, Art Unit 1623

8/8/2008

/Shaojia Anna Jiang, Ph.D./

Supervisory Patent Examiner, Art Unit 1623